

REMARKS

The present communication responds to the Office Action of July 27, 2007. In that Office Action, the Examiner rejected each of the pending claims.

Rejection Under 35 U.S.C. § 103

Claims 1, 30, 32-35, 52 and 64 were rejected under 35 U.S.C. § 103(a) as obvious over the combined teachings from Sierra et al. (WO 98/31403) in view of Peterson (U.S. Patent No. 5,730,933) and further in view of Higgins (U.S. Patent No. 5,753,182). This rejection is traversed at least for the following reasons.

Claim 1 recites “providing a protective atmosphere within the package, wherein providing a protective atmosphere within the packaging of the packaged biological material is carried out by at least partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere,” and “sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agent.”

The Examiner asserts, on page 4 of the present Office Action, the following:

- Sierra et al. teach a method to sterilize a collagen based adhesive by first lyophilizing or freeze drying under vacuum and subsequently sterilizing with a gamma irradiation, while keeping the biological material cool.
- Peterson teaches a method of radiation sterilization of a biological material, wherein prior to sterilization said material is subjected to vacuum or inert gaseous atmosphere of argon, helium, nitrogen (nitrogen is reducing atmosphere and argon is inert) and said material is held in a sealed or unsealed packet during sterilization.

- Higgins teaches sterilization of a prepackaged biological material, wherein said biological material is packaged in an atmosphere of hydrogen.

The Examiner concludes: "In response to applicants' arguments against the references individually, one cannot show non-obviousness by attacking references individually where the rejections are based on combinations of references."

The Applicants respectfully note that, to address the obviousness rejection of the claims, it is necessary to address each reference individually before addressing the teachings of the references in combination.

None of the cited references, alone or in combination, disclose, teach, or suggest "sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agents," as recited by independent claim 1. The Examiner appears to rely on Peterson or Higgins to teach a protective atmosphere comprising a reducing atmosphere. The Applicants respectfully disagree with the Examiner's interpretation of Peterson and Higgins and/or their application to the pending claims.

Notably, the Examiner asserts that "Peterson teaches a method of radiation sterilization of a biological material, wherein prior to sterilization said material is subjected to vacuum or inert gaseous atmosphere of argon, helium, nitrogen (*nitrogen is reducing atmosphere* and argon is inert) and said material is held in a sealed or unsealed packet during sterilization." *Current Office Action, page 4, emphasis added.* The Examiner's assertion that nitrogen is a reducing atmosphere is contrary to the teachings of both Peterson and the present application.

Peterson discloses:

In an alternative embodiment of the present invention, prior to irradiation, the protected mixture is subjected to vacuum or an inert gaseous atmosphere such as nitrogen, argon, helium, neon, and the like. It has been found that the stability of the biologically active compound improves when subjected to an inert or less reactive gases during irradiation treatment. Preferably, the protected mixture is exposed to a vacuum, nitrogen, or argon atmosphere.

Peterson, Col. 5, ll. 28-35. Accordingly, Peterson describes nitrogen as an inert gas. Similarly, the present application discloses, "Inert gases that can be utilized include helium, neon, argon, krypton, xenon, nitrogen, and carbon dioxide." *US 2004/0048371, para. 0034.* Peterson does not disclose, teach, or suggest "replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere," and "sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agents," as recited by independent claim 1. Nowhere does Peterson describe providing a protective atmosphere that comprises a reducing atmosphere or a mixture of reducing atmosphere and inert atmosphere. Rather, the disclosure in Peterson is explicitly limited to providing an inert gaseous atmosphere. If the Examiner intends to take official notice of nitrogen as a reducing atmosphere, the Applicants respectfully request documentary support for such notice, especially given that the teachings of both the prior art and the present application characterize nitrogen as an inert atmosphere.

Higgins teaches sterilizing followed by pressurizing with gas such as hydrogen:

The packaged component is sterilized through radiation. A preferred (but not exclusive) method of irradiating the component is through exposure to gamma rays. The packaged and irradiated component is then positioned in a pressure vessel. A pressurized gas, such as hydrogen, is then introduced into the vessel at a pressure above one atmosphere. Gas pressure and exposure time are controlled so as to allow adequate diffusion of the gas into the component, forcing the hydrogen and free radicals to combine, thus reducing the number of free radicals. The component is removed from the pressure vessel following the selected amount of time, the amount of time and the pressure of the vessel being dependent upon the density of free radicals in the component following irradiation.

Higgins, Col. 3, ll. 25-38. Thus, Higgins explicitly teaches pressurizing the material with hydrogen *after* irradiation. Accordingly, Higgins cannot be interpreted as disclosing, teaching, or suggesting "replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere," and "sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agents," as recited by independent claim 1.

Thus, the Applicants respectfully submit that none of the references teach “replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere,” and “sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agents,” as recited by independent claim 1. In the Office Action, the Examiner goes asserts that “although each of the Examiner-cited references by themselves may not teach every component in the same order or manner as claimed in the elected claims under prosecution in the instant application, these references are not relied upon exclusively but in combination.” *Present Office Action, page 5*. The Examiner adds that “no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of each of the ingredients.” *Present Office Action, page 5*.

The Applicants respectfully submit that “sterilizing the packaged biological material in the presence of the protective atmosphere” is not merely additive of the steps of sterilizing a material and, thereafter, pressurizing the material with hydrogen gas. The Applicants have discovered that a reducing atmosphere during sterilization is beneficial:

The advantage to using a reducing atmosphere in the sterilization method herein is that a reducing atmosphere can help to neutralize destructive species that originate from within the irradiated biological material itself. Oxygen removal alone cannot address damage from these sources. A further advantage of using a reducing atmosphere is its ability to easily diffuse throughout most biological materials and therefore be present at the sites of radical formation, even in solidly frozen objects or high density objects such as donor bone for implantation.

US 2004/0048371, para. 0050. Further, the Applicants respectfully submit that “sterilizing the packaged biological material in the presence of the protective atmosphere,” does not comprise rearrangement of steps or combining old ingredients. None of the references disclose in any way sterilizing in the presence of a protective atmosphere. At best, the references may disclose sterilizing and, separately, a protective atmosphere.

None of Sierra et al., Peterson, or Higgins, alone or in combination, disclose, teach, or suggest a method of sterilizing a packaged biological material which comprises “providing a

protective atmosphere within the package, wherein providing a protective atmosphere within the packaging of the packaged biological material is carried out by at least partially removing an original atmosphere under vacuum, and replacing the original atmosphere with a reducing atmosphere or a mixture of an inert atmosphere and a reducing atmosphere,” and “sterilizing the packaged biological material in the presence of said protective atmosphere effective to reduce and/or inactivate an adventitious agent or adventitious agents,” as recited by claim 1.

Accordingly, it is respectfully submitted that none of Sierra et al., Peterson, or Higgins, alone or in combination, make obvious claim 1. As each of the remaining claims depends either directly or indirectly from claims 1, it is respectfully submitted that none of Sierra et al., Peterson, or Higgins, alone or in combination, make obvious these claims. Accordingly, reconsideration and allowance are respectfully requested.

CONCLUSION

This application now stands in allowable form and reconsideration and allowance is respectfully requested.


This response is being submitted on or before September 27, 2007 making this a timely response. It is believed that no additional fees are due in connection with this filing. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

Respectfully submitted,

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